REMARKS

The rejection of Claims 1-6 under 35 U.S.C. § 102(b) as anticipated by U.S. 5,648,351 (Kelly et al) is respectfully traversed. Kelly et al discloses a broad genus of macrolide compounds for preventing or treating cerebral ischemic disease. The Examiner relies on a particular species thereof disclosed, i.e., tacrolimus, otherwise known as FK506. However, the presently-recited compound of formula (I) is **not** FK506. Using formula (I) as disclosed in Kelly et al, while in FK506, R^{10} is allyl, in the present compound (compound (I)), R^{10} is 2-oxopropyl.

The above is sufficient to demonstrate that the anticipation rejection is incorrect. Nor is the present invention otherwise unpatentable over Kelly et al. Unlike FK506, compound (I) not only significantly protects against brain damage, but it has effectively no immunosuppressive activity. When preventing and/or treating brain damage, immunosuppressive activity is not necessary, but rather may cause some side effect. Therefore, a drug that has no immunosuppressive activity is quite superior to a corresponding drug that has immunosuppressive activity.

The above is demonstrated by a comparative test between compound (I) and FK506 for both immunosuppressive activity and neuroprotective efficacy:

(1) Mixed lymphocyte reaction (MLR)

MLR test is well known and conventional as a test for evaluating immunosuppressive activity of test compounds. In the present experiment, it was performed in a manner similar to that described in U.S 4,929,611 (Okuhara et al). The results are shown in Table 1.

(2) Neuroprotective efficacy on neuronal damage

Table 1 shows the results described in Example 1 of the above-identified application, based on the method described therein for measuring protected area of cortex, for compound (I). Similar data for FK506 had already been obtained.

Table 1

	MLR IC_{50} (nM)	Protected area of cortex (1 $mg.kg^{-1}$)
FK506	< 2	> 60%
Compound (I)	> 100	> 60%

The above results indicate that the compound (I) of the present invention significantly protects brain damage and that it, however, was found to have no immunosuppressive activity.

For all the above reasons, it is respectfully requested that the rejection over Kelly et al be withdrawn.

The rejection of Claims 1, 2 and 6 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. All the claims now contain the limitations of at least Claim 4, not subject to this rejection. Accordingly, it is respectfully requested that it be withdrawn.

The rejection of Claims 1 and 6 under 35 U.S.C. § 101 is now moot in view of the above-discussed amendment. Accordingly, it is respectfully requested that it be withdrawn.

The objection to Claims 4 and 5 is now moot in view of the above-discussed amendment. Accordingly, it is respectfully requested that it be withdrawn.

Regarding the Information Disclosure Statement filed May 17, 2002, discussed at page 2, lines 1-2 of the Office Action, it is noted that the Examiner has lined out the reference designated as "AW." The references cited in this IDS were the references cited in the International Preliminary Examination Report (IPER) in the corresponding international application, which IPER is of record herein. The Examiner could have easily ascertained that the date of this reference is 1999. Nevertheless, **submitted herewith** is a new Form PTO-1449 containing a more complete description of this reference. In addition, the IDS also includes a copy of U.S. 5,376,663 (Cooper et al), described in the specification herein at page 2, below the formula, and above-discussed Okuhara et al. The Examiner is respectfully

requested to initial the Form PTO 1449 submitted therewith, and include a copy thereof with the next Office communication.

All of the presently-pending claims in this application are now believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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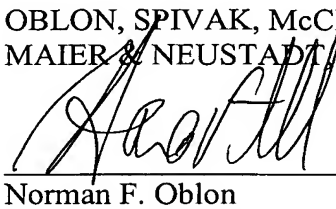

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